

L35 ANSWER 221 OF 272 HCAPLUS COPYRIGHT 2006 ACS on STN  
ACCESSION NUMBER: 1989:497727 HCAPLUS Full-text  
DOCUMENT NUMBER: 111:97727  
TITLE: Novel immunosuppressive fluorinated cyclosporin  
analogs  
INVENTOR(S): Durette, Philippe L.; Kollonitsch, Janos; Pessolano,  
Arsenio A.  
PATENT ASSIGNEE(S): Merck and Co., Inc., USA  
SOURCE: Brit. UK Pat. Appl., 37 pp.  
CODEN: BAXXDU  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 2  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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GB 2207678	A1	19890208	GB 1988-17813	19880726
US 5227467	A	19930713	US 1991-693783	19910429
PRIORITY APPLN. INFO.:			US 1987-81255	A 19870803
			US 1989-298712	B1 19890119

OTHER SOURCE(S):            MARPAT 111:97727  
GI

R10\_R11\_R1\_R2\_R3  
R9  
R8\_R7\_R6\_R5\_R4 I

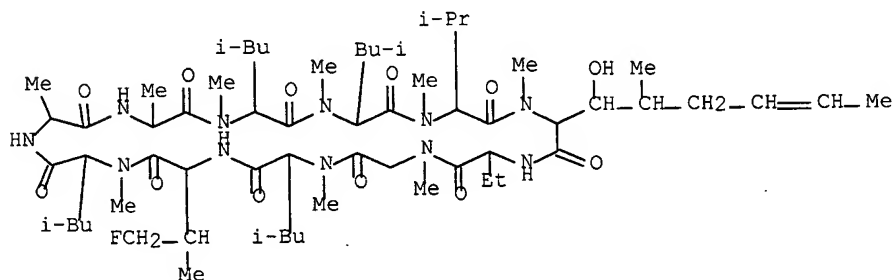
AB Fluorinated cyclosporin analogs [I; R1 = MeBMT or dihydro BMT where BMT = (4R)-4-[(E)-2-butenyl]-4-methyl-L-threonine residue; R2 = Nva, Thr, Ser, or Val, or fluorinated analog thereof; R3 = Sar, D-MeAla; R4, R6, R9, R10 = MeLeu, fluorinated analog thereof; R5 = Val or fluorinated analog thereof; R7 = Ala or fluorinated analog thereof; R8 = D-Ala; R11 = MeVal or fluorinated analog thereof; provided that at least one of R2 to R11 is a fluorinated analog of an amino acid] were prepared as immunosuppressive agents. I (R1 = BMT, R2 = Abu = L-aminobutyric acid, R3 = Sar, R4 = R6 = R9 = R10 = MeLeu, R5 = 4-fluoro-L-valine, R7 = Ala, R8 = D-Ala, R11 = MeVal) was prepared by the solution method and in vitro inhibited mouse T-cell proliferation stimulated with ionomycin plus phorbol myristate acetate with 144% of cyclosporin A's activity.

IT 121893-00-3P 121893-01-4P 121893-02-5P  
121893-03-6P 121893-04-7P 121893-05-8P  
121893-06-9P 121918-44-3P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of, as immunosuppressant)

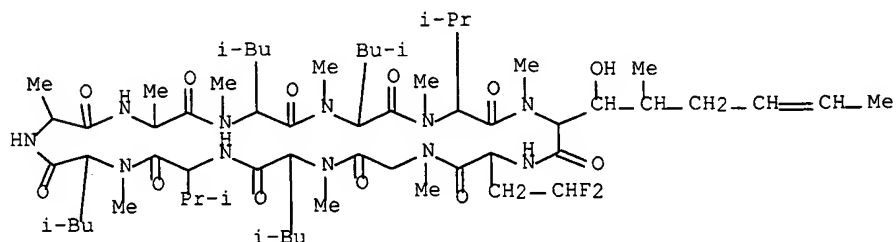
RN 121893-00-3 HCAPLUS

CN Cyclosporin A, 10-(4-fluoro-L-valine)- (9CI) (CA INDEX NAME)

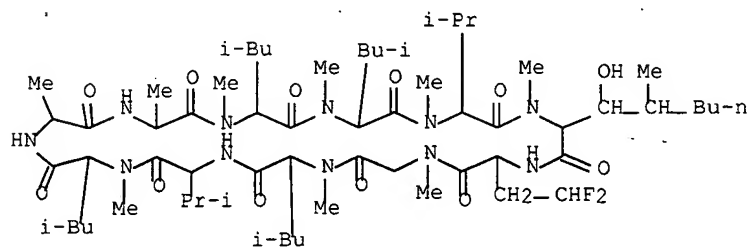


RN 121893-01-4 HCAPLUS

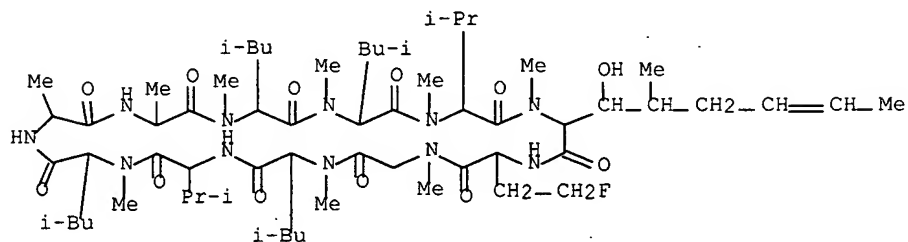
CN Cyclosporin A, 7-(4,4-difluoro-L-2-aminobutanoic acid)- (9CI) (CA INDEX NAME)



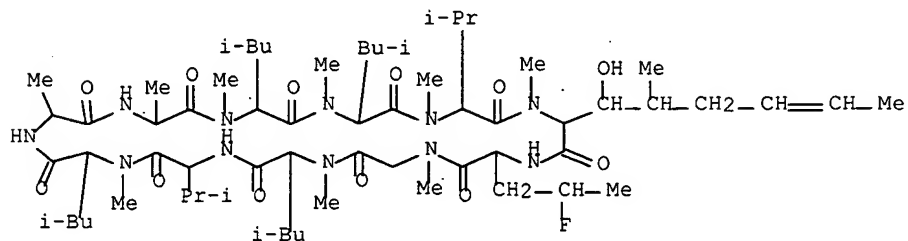
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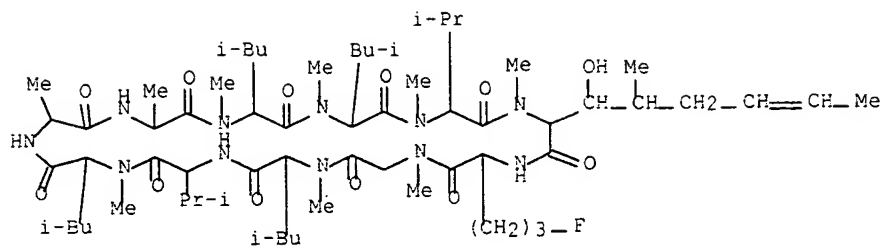
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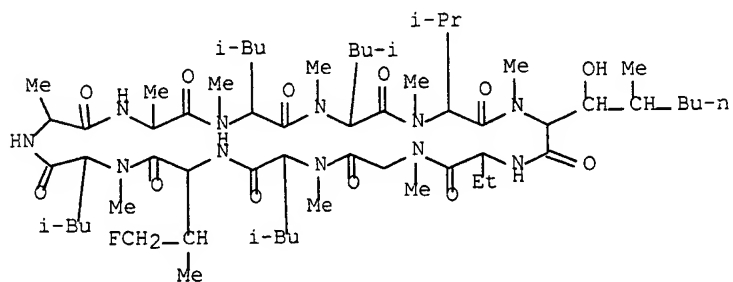
RN 121893-04-7 HCAPLUS  
 CN Cyclosporin A, 7-(4-fluoro-L-norvaline)- (9CI) (CA INDEX NAME)



RN 121893-05-8 HCAPLUS  
 CN Cyclosporin A, 7-(5-fluoro-L-norvaline)- (9CI) (CA INDEX NAME)



RN 121893-06-9 HCAPLUS  
 CN Cyclosporin A, 6-[(3R,4R)-3-hydroxy-N,4-dimethyl-L-2-aminooctanoic acid]-10-(4-fluoro-L-valine)- (9CI) (CA INDEX NAME)



RN 121918-44-3 HCAPLUS  
 CN Cyclosporin A, 5-(4-fluoro-N-methyl-L-valine)- (9CI) (CA INDEX NAME)

